Long-Term Course of Hospitalization for Schizophrenia: Part II. Change With Passage of Time

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Abstract

This analysis examines the notion of progressive deterioration in schizophrenia, using long-term followup data on hospital episodes in defined cohorts from psychiatric case registers in Victoria, Australia; Denmark; and Salford, England. The analyses differentiate heterogeneity existing at the first hospitalization for schizophrenia, which produces a widely varying natural course, from heterogeneity that develops over time, as episodes of hospitalization occur. Episodes of hospitalization for schizophrenia tend to cluster earlier rather than later in the treatment career, suggesting a progressive amelioration rather than deterioration. When overall chronicity is adjusted, each additional episode of hospitalization lowers the risk for a further hospitalization by about 10 percent.

Kraepelin's work seemed to imply that a large proportion of schizophrenic patients would progressively deteriorate over the years following their initial episode (Kraepelin 1919/1971). Progressive deterioration implies that the ultimate outcome is unfavorable and that the rate of deterioration accelerates over time. There has been much controversy as to whether ultimate outcome is unfavorable or not (Harding et al. 1987; Westermeyer and Harrow 1988) but little analysis of the progressive aspect of the course. The notion of progressive deterioration implies that the rate at which episodes occur speeds up as time passes and that the level of functioning to which the individual returns upon remission from a given episode is progressively lower, and the probability of a future episode higher, than before the episode. The shift in level of functioning is portrayed in Ciompi's drawings of typologies of course (Ciompi 1980) and is part of the concept of "shift-like" schizophrenia (Shmaonova et al. 1983). The *DSM-III* states that the "most common course is one of acute exacerbations with *increasing* residual impairment between episodes" (emphasis added; American Psychiatric Association 1980, p. 185), which agrees with many clinical textbooks (e.g., Slater and Roth 1974, p. 308; Lehmann and Cancro 1985, p. 710).

Several lines of reasoning suggest that the rate at which episodes occur should decline with time and the level of functioning should improve with time. For discussion purposes we call these phenomena "progressive amelioration," in contrast to the notion of progressive deterioration. Clinicians with a developmental orientation have noted this possibility (Cohler and Ferrono 1987; Wing 1987). It may be that some patients learn to persist with medication only after several episodes have demonstrated its value. It could be that decline in rate of episodes occurs because the individual learns to recognize initial symptoms of relapse, and thus is able to prevent the episode or lessen its severity (e.g., Herz 1984). It could also be that the patient's family learns to adjust to the schizophrenia only gradually, after some years (Wing 1987). Decline in the potency of schizophrenia is consistent with some biological models of the aging brain (Finch and Morgan 1987). Several reviews of followup studies have

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concluded that progressive amelioration is the correct characterization (Bleuler 1978; Harding et al. 1987; McGlashan 1988). This analysis focuses on the progressive aspect of the course, using data on the rate at which episodes of hospitalization occur from three psychiatric case registers.

Methods

Registers. Three psychiatric case registers, described in Eaton and colleagues (1992, Part I of this article) participated in these analyses: Victoria, Australia; Salford, England; and Denmark. Staff from each of the registers sought permission for participation in the study from their local committees on human subjects. Considerable care was taken to create data files for analysis that were anonymous, so that they could be edited and analyzed at one location, The Johns Hopkins University School of Hygiene and Public Health.

Samples. Cohorts defined for these analyses had at least 16 years of followup after discharge for their first hospitalization for schizophrenia. Sixteen years represented a compromise between a long duration of followup and an entry period long enough to generate sufficient sample size. For the Danish cohort this includes individuals who were discharged from their initial hospitalization for schizophrenia before March 29, 1972, and for the Victoria cohort, the individuals discharged before November 26, 1966. Because the Salford register sample was smaller, only people with a minimum of 14 years of followup were included. The latest date of discharge to start the Salford followup was April 4, 1974.

The two statistical approaches presented below benefit from restricting the samples in slightly different ways. In order to make the results as comparable as possible, we applied restrictions to the cohorts equally for both forms of analysis. The proportional hazards models suffered from outlier episodes in the tail, leading to omission of hospitalizations after 16 years in the Victoria and Denmark data (14 and 16 episodes omitted, respectively) and after 14 years in Salford (4 episodes omitted). The log linear model benefits from having at least five individuals in each stratum of total number of episodes, as described below and shown in table 2. In the Victoria cohort, 14 individuals with more than 13 episodes (range = 14–30) were omitted; in the Denmark cohort, 23 individuals with more than 21 episodes (range = 22–56) were omitted; in the Salford data, 2 individuals with more than 15 episodes (21 and 26) were omitted. The resulting sample sizes were 1,150 for Victoria, 600 for Denmark, and 100 for Salford.

Statistical Analyses. Two operational conceptualizations of the progress of schizophrenia are presented. One focuses on the clustering of episodes of hospitalization over time. In order to model the effects of the distribution of the hospitalizations and to control for gender, decade of onset, and number of hospitalizations before the one diagnosed as schizophrenia, a log linear model was used. A second operational conceptualization of the process focuses on the hazard for rehospitalizations as a function of their occurrence. The logic here is that a decline in the rate of hospitalizations will result in the later hospital episodes for any person being more spread out than earlier hospitalizations. This conceptualization takes advantage of the Cox (1972) proportional hazards model, pooling all hospital episodes within individuals.

There are two unresolved statistical issues in studying the long-term course of schizophrenia: censoring and heterogeneity. The problem of censoring arises because the followup period ends before all hospitalizations for the cohorts have occurred. This problem is handled in the log linear analysis of clustering by following each individual for the identical period of time after initial discharge, no matter when discharge occurs. Censoring is addressed in the proportional hazards model by defining and redefining the risk set, so that only individuals who are actually at risk for a hospital episode contribute to the parameter estimates.

The issue of heterogeneity has been problematic in research on various longitudinal probabilistic processes. Even if the proneness to events is distributed equally across individuals, some individuals can have many events, and some few, within a given period. With equal distribution of proneness, the distribution of events per person will be Poisson (Feller 1968). When the distribution of proneness to events is unequal across individuals, the distribution of events per person will have a longer tail than the Poisson, such as the negative binomial sometimes used to fit accident statistics (Arbous and Kerrich 1951) and also fit to episodes of schizophrenia (Eaton 1974). The central problem is that the effects of progressive deterioration, sometimes called "contagion" in textbooks of probability (Feller 1968), produce the same elongated tail on the distribution of episodes as is produced by an

unchanging heterogeneity. Research on schizophrenia strongly suggests that there is considerable heterogeneity in both severity and chronicity (Carpenter et al. 1985; Carpenter and Kirkpatrick 1988). Earlier work with data from the registers included here suggests, for example, that age of onset is an indicator of this heterogeneity and that those with early onset will have a more chronic course (Eaton et al. 1992, Part I of this article). In the analyses below, we strive to eliminate the effects of preexisting heterogeneity in the population in regard to chronicity, in order to study possible change over time in the tendency to have hospitalizations. The total number of hospital episodes over the entire followup period serves as the best indicator of this heterogeneity, and it is used as a covariate along with other possible indicators for heterogeneity.

Another statistical problem is that hospitalizations are not independent, because each individual can generate more than one over the length of the followup period. The variances produced by generally available log linear and proportional hazards models estimating algorithms (e.g., in SAS Users Guide [1985]) are not robust to the departure from independence, and resulting significance tests are inappropriate. There is a positive correlation of the occurrence of episodes within individuals over time, as implied by the notion of heterogeneity, and the generally available software will produce variances that are too small. In the analyses below we use new estimation algorithms that correct for departure from independence (Liang and Zeger 1986; Zeger and Liang 1986; Wei and Amato 1988) to ensure that our tests are conservative.

Results

There were some differences in the cohorts for the three register areas, as might be expected. Table 1 shows that about half of the patients for Victoria and Salford were males, but that more than 60 percent were male in Denmark. The age of onset was in young adulthood, which is consistent with the literature (Eaton 1985), with the minor exception of a curiously high percentage of onset after the age of 60 in Salford.

The Danish cohort was more chronic than the other two, consistent with earlier analyses of hospitalization following first discharge in much larger cohorts (Eaton et al. 1992, Part I of this article). A higher percentage of the Danish cohort had hospitalizations before the one in which the case first received the diagnosis of schizophrenia (over 15% vs. under 8.5% for Victoria and Salford). Individuals in the Danish cohort had many more hospitalizations during the followup: almost 25 percent had seven or more hospitalizations, compared with 5.5 percent for Victoria, with identical length of followup, and 11.0 percent in Salford, where the followup was 2 years shorter. The mean numbers of hospitalizations for Victoria, Denmark, and Salford, respectively, are 2.5, 5.3, and 3.3 (data not shown).

Table 2 presents the distribution of hospital episodes in periods following the first discharge for the Danish cohort. Each period in table 2 (columns) is exactly 2 years long for each individual, regardless of the exact date of the first discharge. The rows of the table represent total number of hospitalizations after the first. Similar tables were constructed for the Victoria and Salford cohorts, but there were inadequate cell sizes for the Salford cohort.

The question is how hospitalizations are spread over time. For example, there were 68 individuals who had two more admissions after the first one in which they were diagnosed with schizophrenia. This totals 132 hospital episodes, 61 (46%) of which occurred within 2 years after the first discharge, 16 (12%) in years 3 and 4, 15 (11%) in years 5 and 6, and so on. The stratum with 14 hospitalizations, which comprised six individuals, had 14 percent in the first 2-year period, 14 percent in the second 2-year period, and so on.

Table 2 shows that hospital episodes clustered early in the psychiatric career. The distribution of hospitalizations over time, as shown in table 2, can be fit to a log linear model for a more precise description. This allows holding constant the effects of gender, onset decade, number of prior hospitalizations before being diagnosed as having schizophrenia, and total number of hospitalizations. Table 3 presents the adjusted odds of having a hospitalization in each interval, compared to the first interval, and shows that the tendency to have episodes of hospitalization declined with time in the Victoria and in the Denmark data. The odds of a hospitalization occurring in the final 2-year period were about one-quarter the odds of a hospitalization occurring in the same initial 2-year period as the first hospitalization. The decline appears to be most dramatic in the initial 2 years (from 1.00 to 0.57 and to 0.66 for Denmark and Victoria, respectively) and more gradual thereafter.

It is necessary to consider whether the decline in numbers of hospital episodes, shown in table 3, could have been produced by sampling variation. The observations for the analysis are not drawn independently, but rather are clustered within

Table 1. Descriptive statistics for all first hospitalizations of subjects who ever received a diagnosis of schizophrenia and had a minimum of 16 years of followup[1]

Characteristic	Victoria, Australia	Denmark	Salford, England
Gender (%)			
Male	49.9	63.8	50.0
Female	50.1	36.2	50.0
Age of onset (%)			
10–19	8.2	17.7	12.0
20–29	29.0	43.0	34.0
30–39	27.4	14.2	10.0
40–49	18.8	10.5	19.0
50–59	10.2	7.8	13.0
60+	6.4	6.8	12.0
Number of prior hospitalizations (%)			
0	91.5	83.8	93.0
1	7.4	12.3	3.0
2	0.8	3.5	2.0
3+	0.3	0.4	2.0
Number of hospitalizations after first schizophrenia diagnosis (%)			
0	51.1	25.2	36.0
1	18.6	12.8	22.0
2	9.6	11.3	17.0
3	5.5	8.8	5.0
4	4.3	6.7	6.0
5	3.0	5.3	2.0
6	2.4	5.2	1.0
7+	5.5	24.7	11.0
Total *n* of cases	1,150	600	100
Total *n* of hospitalizations	2,866	3,193	327

[1]For Salford, a minimum of 14 years of followup.

individuals. Usually, but not always, variances for clustered observations are larger than variances for independent observations, due to positive correlation within the cluster and reduced effective sample size. Therefore, the method of Liang and Zeger (1986) was used to estimate variances that were robust to the effect of within-individual clustering. The structure of the covariance matrix of episodes was assumed to be autoregressive with a lag of 2, as suggested in earlier research on the course of schizophrenia (Eaton 1974). The resulting 95 percent confidence intervals are shown in table 3. None of the confidence intervals overlaps with 1.00, and it appears that the decline in numbers of hospitalizations was not due to chance.

Because the decline in risk for rehospitalization appears to be greatest in the first two periods, these were analyzed on a month-by-month basis as shown in figures 1, 2, and 3. Each of these figures shows a different stratum for Denmark, defined by numbers of hospitalizations: figure 1 for those with 2 hospitalizations; figure 2 for those with 3 hospitalizations; and figure 3 for those with 10 hospitalizations. The figures show that the modal month for rehospitalization is the first month following discharge. After this time, it is hard to see a pattern. Similar results were observed in the Victoria data. Across the strata defined by total number of

Table 2. Temporal distribution of rehospitalizations: Denmark, 1970–1988[1]

Total number of hospitalizations after first discharge	1–2	3–4	5–6	7–8	9–10	11–12	13–14	15–16	Total number of Episodes (2,591)	Total number of Patients (600)
0	—	—	—	—	—	—	—	—	—	151
1	45 (58)	8 (10)	10 (13)	3 (4)	2 (3)	0 (0)	3 (4)	6 (8)	77	77
2	61 (46)	16 (12)	15 (11)	9 (7)	9 (7)	10 (7)	8 (6)	8 (6)	132	68
3	49 (31)	19 (12)	21 (13)	15 (9)	15 (9)	12 (8)	12 (8)	16 (10)	159	53
4	59 (37)	23 (14)	14 (9)	15 (9)	8 (5)	11 (7)	15 (9)	15 (9)	160	40
5	55 (34)	35 (22)	18 (11)	11 (7)	14 (9)	10 (6)	8 (5)	9 (6)	160	32
6	51 (27)	27 (15)	28 (15)	27 (15)	17 (9)	15 (8)	9 (5)	12 (6)	186	31
7	35 (22)	36 (22)	29 (18)	29 (18)	11 (7)	7 (4)	4 (2)	10 (6)	161	23
8	36 (26)	19 (14)	20 (15)	19 (14)	10 (7)	10 (7)	6 (4)	16 (12)	136	17
9	32 (27)	21 (18)	17 (14)	19 (16)	10 (8)	3 (3)	6 (5)	9 (8)	119	13
10	42 (25)	27 (16)	19 (11)	25 (15)	19 (11)	9 (5)	9 (5)	20 (12)	170	17
11	27 (14)	31 (17)	33 (18)	24 (12)	16 (9)	19 (10)	13 (7)	24 (13)	187	17
12	23 (21)	11 (10)	14 (13)	13 (11)	14 (12)	13 (13)	12 (10)	8 (7)	108	9
13	31 (27)	21 (18)	13 (11)	23 (20)	7 (6)	10 (9)	4 (3)	8 (7)	117	9
14	12 (14)	12 (14)	11 (13)	12 (14)	10 (12)	17 (20)	5 (6)	5 (6)	84	6
15	10 (13)	6 (8)	9 (12)	10 (13)	18 (24)	9 (12)	6 (8)	7 (9)	75	5
16	42 (22)	31 (16)	29 (15)	35 (18)	10 (5)	21 (11)	14 (7)	10 (5)	192	12
17	22 (18)	9 (8)	9 (8)	22 (18)	16 (13)	21 (17)	10 (8)	10 (8)	119	7
18	11 (20)	7 (13)	4 (7)	10 (19)	6 (11)	9 (17)	7 (13)	0 (0)	54	3
19	10 (11)	9 (9)	15 (16)	23 (24)	18 (19)	10 (11)	10 (11)	0 (0)	95	5
20	25 (25)	20 (20)	22 (22)	21 (21)	5 (5)	0 (0)	0 (0)	7 (7)	100	5

[1]Number of hospitalizations (percentages in parentheses), after the first, within 2-year periods following discharge from first hospitalization for schizophrenia.

hospitalizations, the mode was usually, but not always, in the first month after discharge. The data in table 3 show that there is a decline in the rate of rehospitalization, which is spread out over 16 years but has a slight tendency to occur most forcefully in years 3 and 4 following discharge; the data in figures 1, 2, and 3, and comparable data for Victoria show that rehospitalizations that occur during the first 4 years tend to be concentrated in the first month after discharge.

If hospital episodes are less likely to occur later in the psychiatric career, then lengths of stay in the community, outside the hospital, should be correspondingly longer. Figures 4, 5, and 6 show box plots (McGill et al. 1978) for lengths of stay in the community following discharges occurring during each of the 2-year intervals following first discharge for the Victoria, Denmark, and Salford cohorts, respectively. The plots indicate a tendency for the duration of community tenure to lengthen. For example, in Victoria (figure 4) the median tenure in the community following a discharge occurring in the first 2-year period after the initial episode is 220 days, whereas the median tenure in the community for discharges occurring in years 15 or 16 following the initial episode is 533 days. A similar tendency is evident in Denmark and in Salford. In all three systems, the 75th percentile is markedly higher later in the followup period (e.g., for Victoria, 402 days in the first followup period and 1,662 days in the eighth followup period).

The analyses are compromised because length of stay in the community could not have a value extending beyond the end of the followup period. To *minimize the effects of* this censoring, we entered into the

Table 3. Log linear models of the distribution of episodes into 2-year periods after first discharge[1]

Number of years following first hospitalization	Odds	95% confidence interval
	Denmark	
1-2	1.00	
3-4	0.57	(0.49-0.66)
5-6	0.52	(0.43-0.61)
7-8	0.54	(0.44-0.65)
9-10	0.35	(0.28-0.42)
11-12	0.32	(0.26-0.39)
13-14	0.24	(0.19-0.30)
15-16	0.29	(0.23-0.37)
	Victoria, Australia	
1-2	1.00	
3-4	0.66	(0.56-0.78)
5-6	0.59	(0.48-0.71)
7-8	0.42	(0.34-0.52)
9-10	0.41	(0.33-0.51)
11-12	0.38	(0.30-0.47)
13-14	0.34	(0.27-0.44)
15-16	0.24	(0.19-0.33)

[1]Odds for hospitalization in that interval, compared with the first 2-year period, adjusted by age of first onset, gender, number of hospitalizations before initial hospital diagnosis of schizophrenia, and total number of hospitalizations following first hospital diagnosis of schizophrenia.

plots only community tenures before the beginning of a final episode of hospitalization that actually was recorded during the followup period (i.e., the box plots are based on 1,716, 2,593, and 227 episodes in Victoria, Denmark, and Salford, respectively). In Salford and Denmark, it appears that the length of stay in the community was diminishing during the final 2 years of followup. We interpret this as an effect of eliminating the censored observations from the data, in that longer lengths of stay in the community were more likely to be omitted. These omissions may have produced the diminishing trends in the final years of followup. It is also possible that the diminution in the final years results from developmental processes. For example, 13 to 16 years after discharge from the initial hospital episode, most persons diagnosed with schizophrenia will be in late middle age. During this period there may be a rise in the possibility of rehospitalization due to death of parents who had protected the patient until this time.

Estimating length of tenure in the community toward the end of the followup period is problematic because many individuals are still in the community at the end of the followup, and the duration for that period is biased low. The proportional hazard approach deals appropriately with this problem by censoring lengths of stay that are continuing at the end of followup. This approach has the form of a regression, and each day of followup is included in the estimation of regression coefficients until the community tenure concludes with a hospitalization, a death, or until the end of the followup period, in which case the length is censored. Variables that may have an independent effect on the risk for rehospitalization following discharges throughout the course, including gender, age of onset, number of hospital episodes before the initial diagnosis of schizophrenia, and total number of hospitalizations during the followup are also held constant (table 4).

Gender, age at first onset, and number of hospitalizations before the initial hospital diagnosis of schizophrenia do not have strong and consistent effects on the course of hospitalization (table 4). Later age of onset is associated with a more benign course in Victoria and Denmark. These results are similar to those of previous research with these data on the hazard of rehospitalization after the first discharge (Eaton et al. 1992, Part I of this article), except that the effects of age of onset were stronger in the previous work. In that analysis there was no adjustment for total number of hospitalizations, which may be a more powerful indicator of the chronicity/severity variable. In these cohorts, earlier age of onset is a strong and significant predictor of rehospitalization risk until the total number of episodes is entered into the model (data not shown).

Individuals with a greater total number of hospitalizations have a higher risk for readmission. For example, in Victoria, individuals with two episodes have a 33 percent higher risk for readmission than individuals with one; those with three episodes have a 33 percent higher risk for readmission than those with two; and so forth. The limitation of the followup period constrains this

Figure 1. Denmark: Individuals who had one hospitalization after first discharge

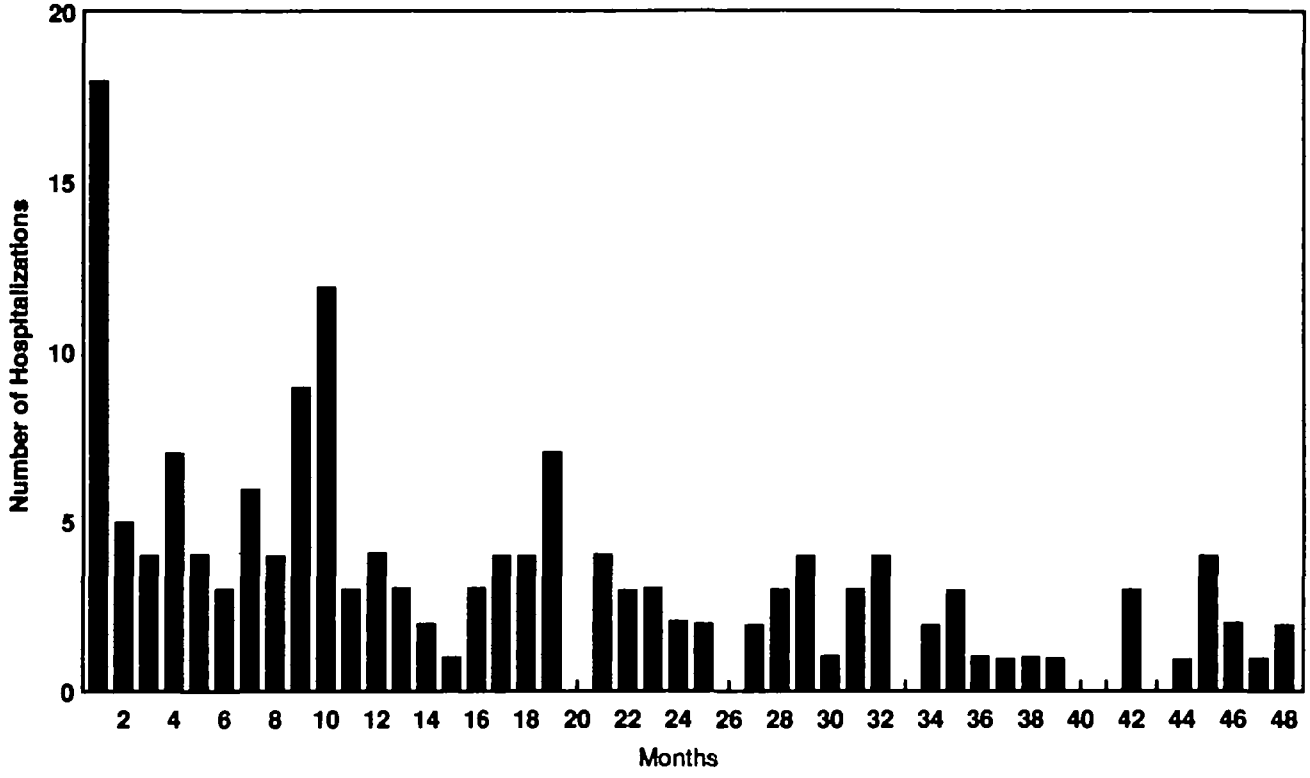


Figure 2. Denmark: Individuals who had two hospitalizations after first discharge

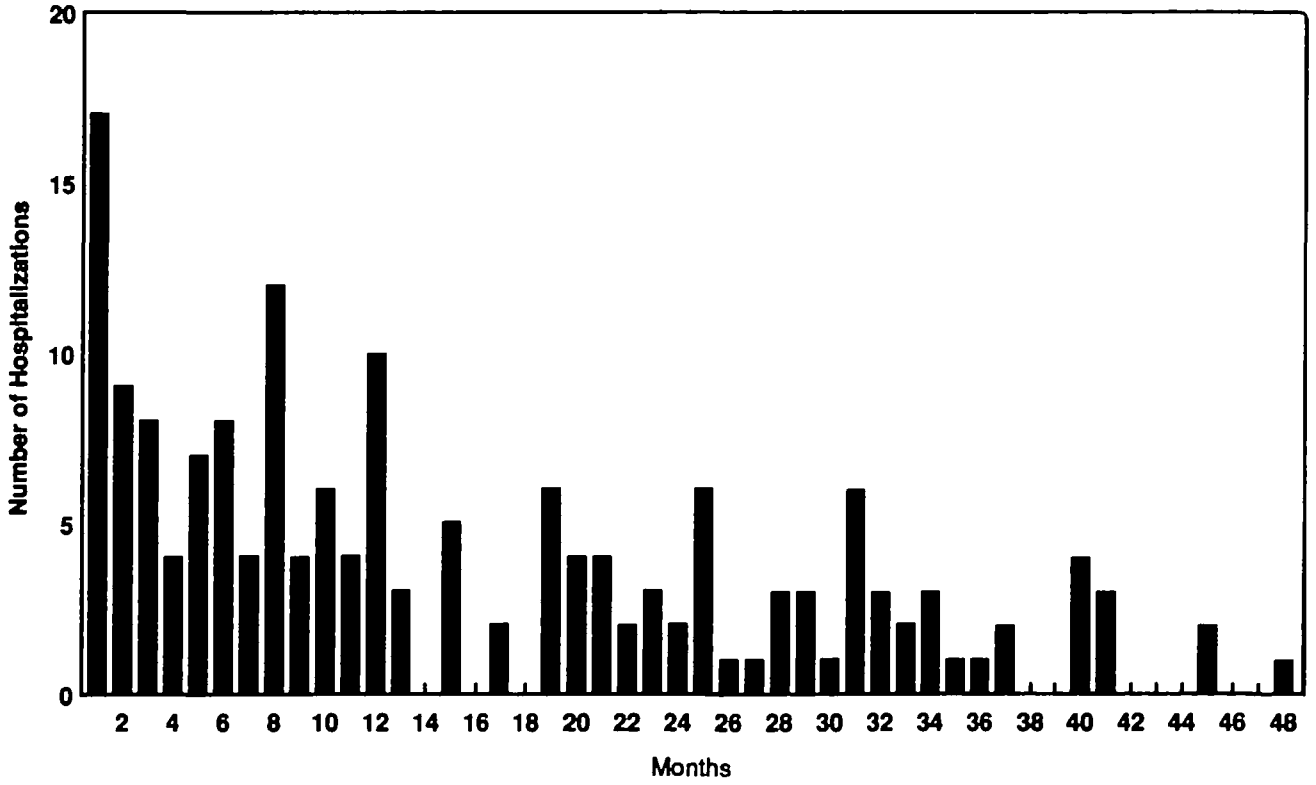


Figure 3. Denmark: Individuals who had nine hospitalizations after first discharge

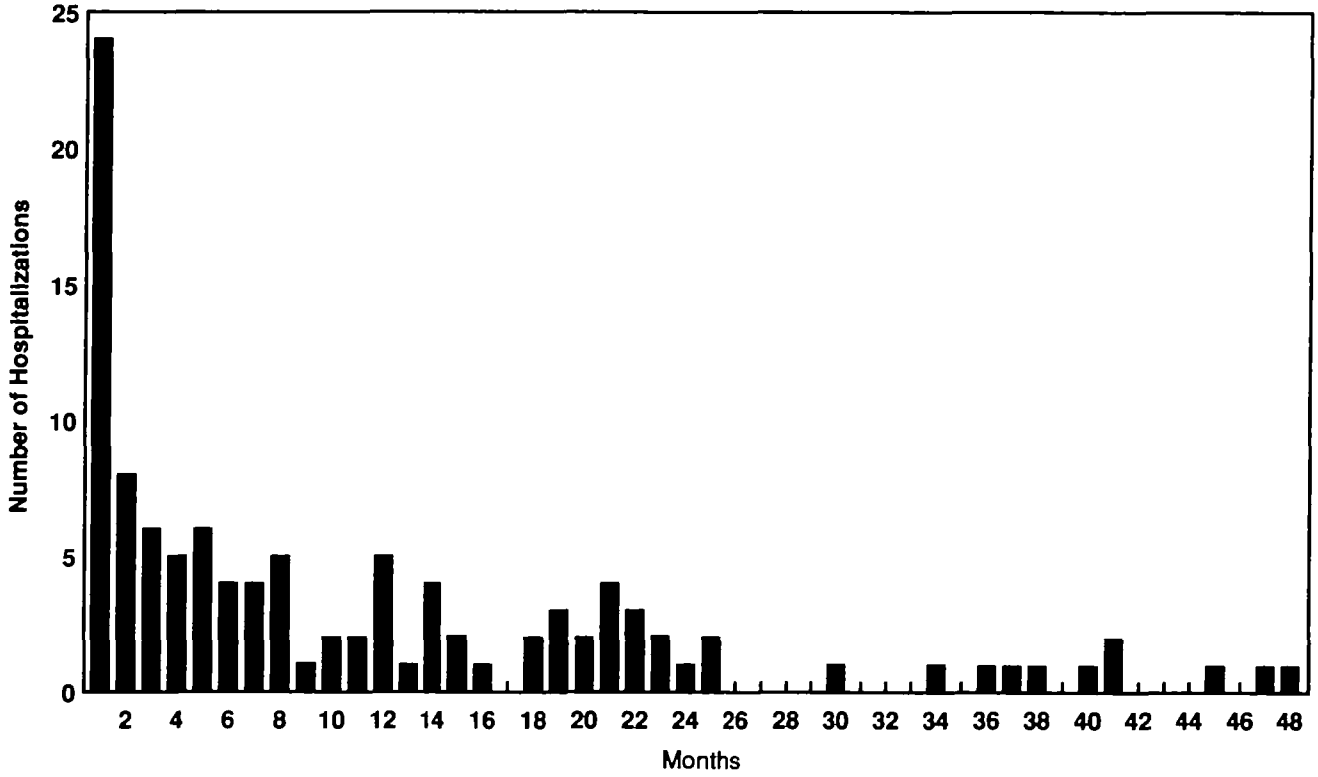
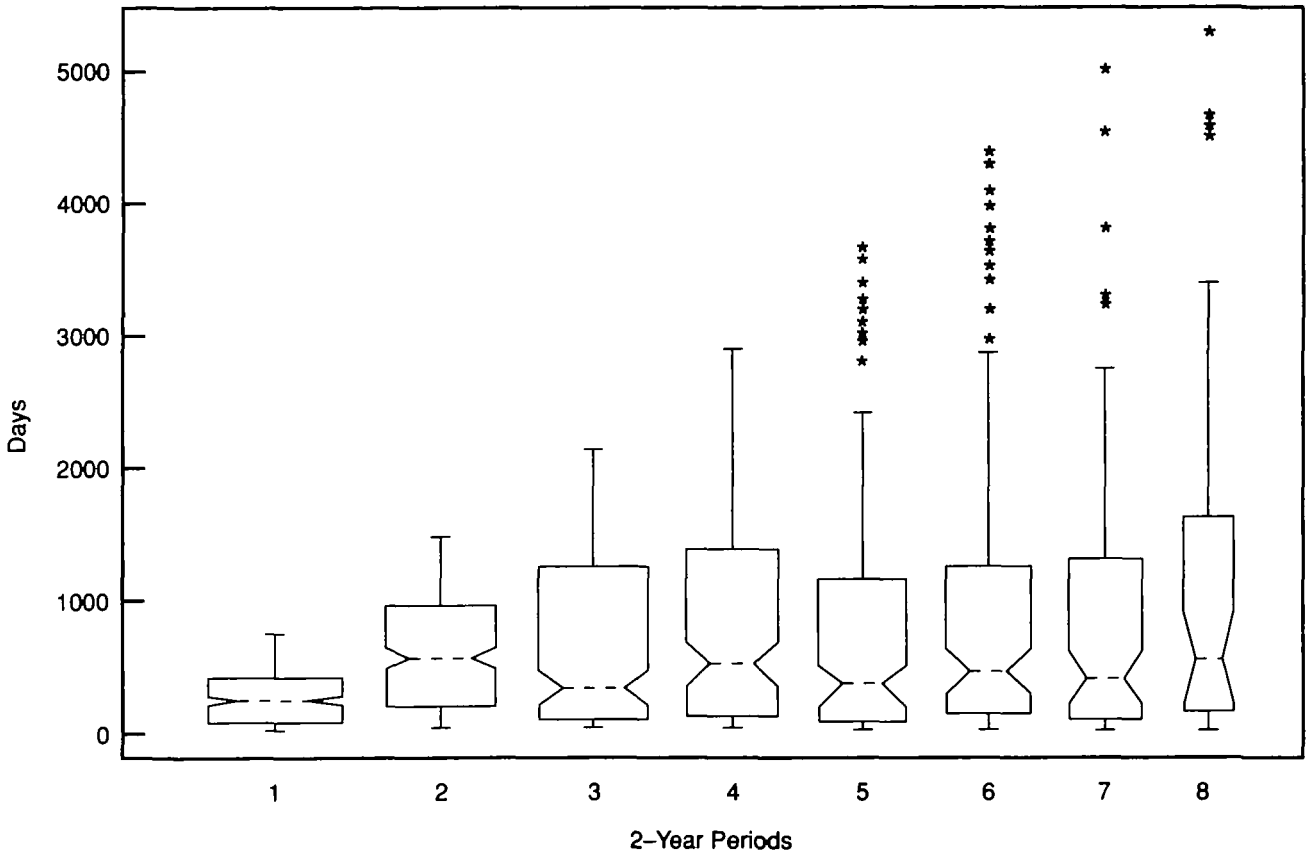


Table 4. Proportional hazard models: Estimated relative risks (95% confidence interval) of all re-hospitalizations after first hospital diagnosis of schizophrenia for 16 years of followup[1]

Characteristic	Victoria, Australia	Denmark	Salford, England
Gender			
Male	1.00	1.00	1.00
Female	1.01 (0.86-1.19)	0.97 (0.79-1.18)	0.72 (0.57-0.90)
Age of onset at first hospitalization for schizophrenia			
10-19	1.00	1.00	1.00
20-29	0.87 (0.63-1.19)	0.91 (0.79-1.16)	0.94 (0.70-1.28)
30-39	0.90 (0.66-1.21)	0.91 (0.64-1.28)	0.85 (0.61-1.18)
40-49	0.87 (0.63-1.20)	0.71 (0.54-0.92)	1.23 (1.12-1.23)
50-59	1.01 (0.76-1.34)	0.77 (0.57-1.05)	1.58 (0.92-2.71)
60+	0.63 (0.42-0.94)	0.80 (0.57-1.11)	0.77 (0.34-1.76)
Number of hospitalizations before first hospital diagnosis of schizophrenia	1.08 (0.89-1.31)	0.98 (0.83-1.14)	0.92 (0.68-1.24)
Total number of hospitalizations for the individual during followup[2]	1.33 (1.28-1.37)	1.13 (1.11-1.16)	1.23 (1.17-1.29)
Each additional hospitalization	0.89 (0.87-0.91)	0.95 (0.94-0.96)	0.93 (0.87-0.99)
Total number of hospitalizations	2,866	3,193	327

[1]For Salford, 14 years of followup.
[2]Following the hospitalization on which the diagnosis of schizophrenia was first received.

Figure 4. Box plot of time between hospitalizations in Victoria



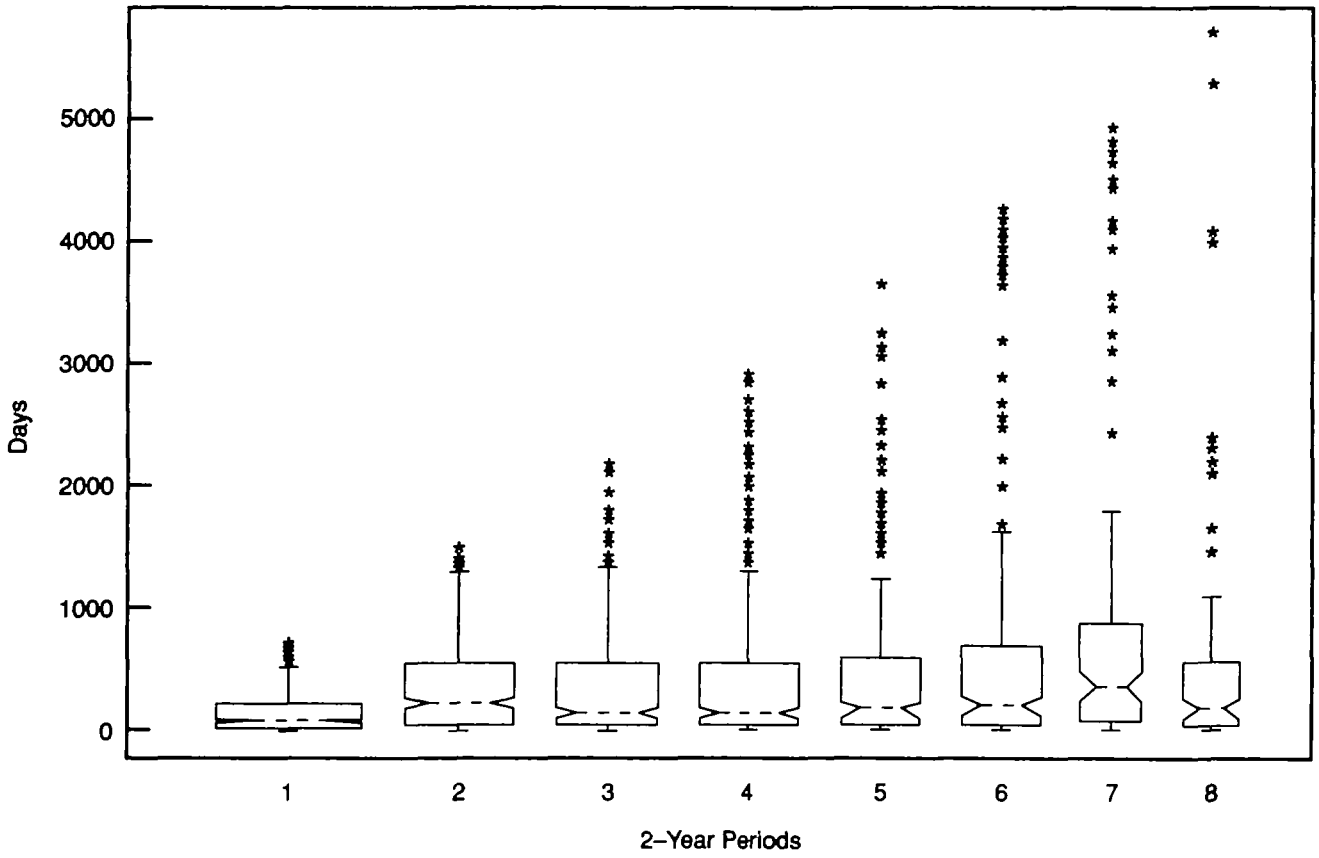
The top of the box is the 75th percentile for length of community tenure, the bottom of the box is the 25th percentile, and the median is the line drawn through the box. The width of the box is proportional to the square root of the sample size of episodes occurring in the pertinent period of time, and notches indicate the 95 percent confidence interval for the median.

effect to have this shape, in that if more hospitalizations have to be fit into the same duration of followup, the risk for readmission must perforce be greater. This variable is included in the model to control for heterogeneity of severity. Holding constant this indicator of severity, does the rapidity with which hospital episodes occur change over time? This issue is addressed by the relative risks for each additional hospitalization, which are less than 1.00, indicating a decline in the force producing hospitalizations as the career proceeds. Each additional hospital episode reduces the risk for rehospitalization by about 7 percent.

In the proportional hazard model in table 4, the focus was on the change in risk with each additional hospitalization. The focus could as well have been on the amount of time since discharge from initial hospitalization. Similar models were estimated substituting "years since first discharge" for the "additional hospitalization" variable. Results were very similar: they were consistent across the three sites, had equal statistical significance, and had small to modest effects (about 3% reduction in risk for each year following discharge).

The results presented in the proportional hazards models in table 4 are consistent with results in table 3 and with the plots in figures 4, 5, and 6. But as with the log linear models in table 3, tests of significance based on independent sampling are not appropriate because each in-

Figure 5. Box plot of time between hospitalizations in Denmark

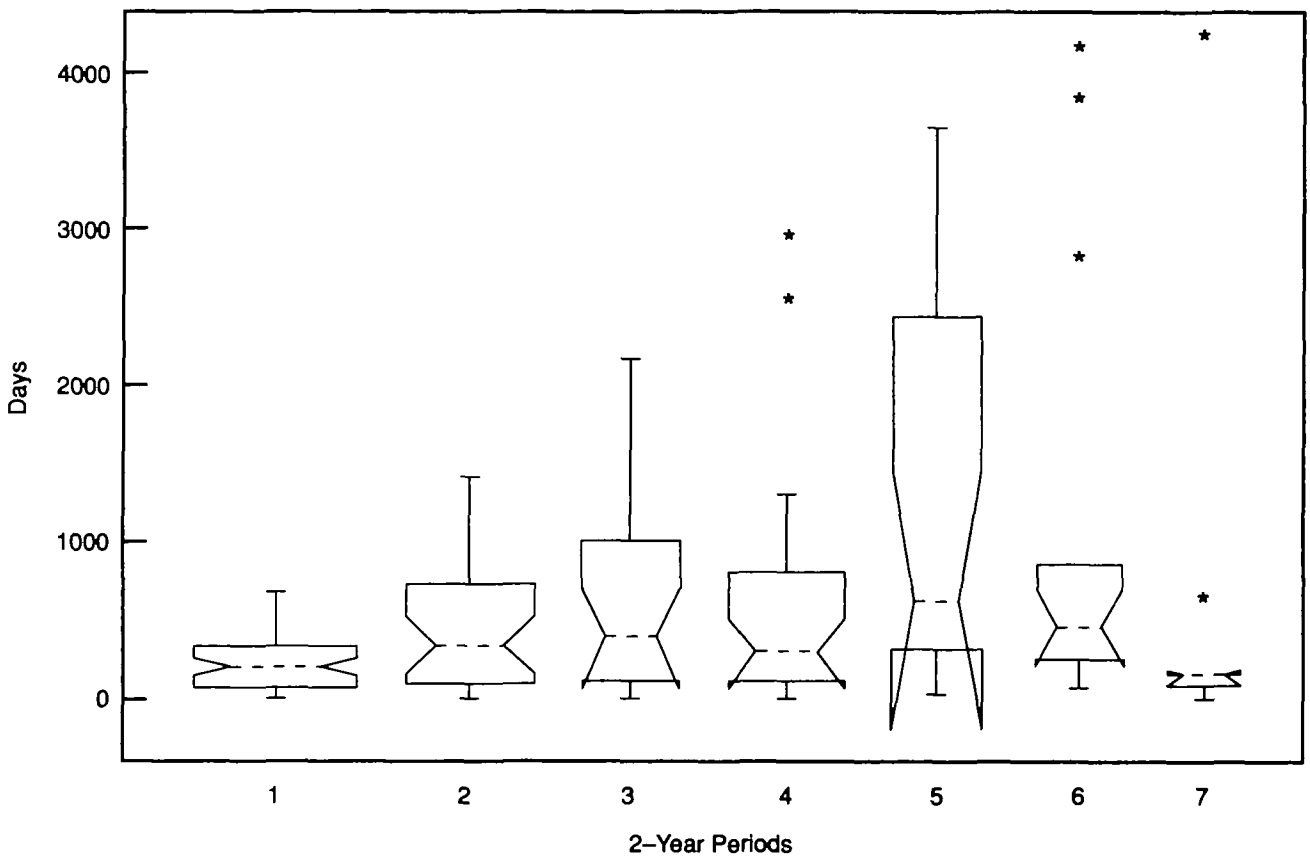


The top of the box is the 75th percentile for length of community tenure, the bottom of the box is the 25th percentile, and the median is the line drawn through the box. The width of the box is proportional to the square root of the sample size of episodes occurring in the pertinent period of time, and notches indicate the 95 percent confidence interval for the median.

dividual can contribute more than one observation to the data. Therefore, in estimating the 95 percent confidence intervals shown in table 4, a method developed by Wei and Amato (1988) was used, which takes account of the intraindividual variation in a fashion analogous to that developed for the generalized linear models by Zeger and Liang (1986). In each of the three cohorts, the 95 percent confidence interval for the odds ratio for each additional hospital episode does not include 1.00, indicating that the results are unlikely to be due to chance variation.

The decline in tendency to have hospitalizations would not have been revealed in table 4 if the total number of hospital episodes during the followup, which we used as an indi cator of overall severity and chronicity, had not been a covariate. Had we not adjusted by total number of hospitalizations, the analysis might have revealed a higher risk for rehospitalization following, say, the sixth as compared to the fourth episode. The problem in this comparison is that individuals who have had six hospital episodes are more severely and chronically ill than those who have had four. Individuals with six hospitalizations had them more rapidly because the followup periods for those with six and those with four were identical. Separate models could be displayed for each of several strata defined by the total number of hospital episodes, but the results across the strata are very similar to those in table 4.

Figure 6. Box plot of time between hospitalizations in Salford



The top of the box is the 75th percentile for length of community tenure, the bottom of the box is the 25th percentile, and the median is the line drawn through the box. The width of the box is proportional to the square root of the sample size of episodes occurring in the pertinent period of time, and notches indicate the 95 percent confidence interval for the median.

Discussion

These analyses show that the tendency to have episodes of psychiatric hospitalization declines after an initial hospitalization for schizophrenia. The data were analyzed with two distinct statistical approaches and are displayed in graphic form. The results do not appear to be due to chance variation. The findings are consistent in cohorts of first-admitted schizophrenic patients in three different countries. These are the first analyses of long-term followup using newly developed statistical technologies that take into account censoring and clustering. The general tendency for amelioration is fundamentally contrary to early concepts of progressive and inevitable deterioration but may have resulted from a change in the nature of schizophrenia since early research on the course of the disease (e.g., Shepherd's [1989] review).

One explanation for the decline in rate of rehospitalization could be a change in the administrative structure of the hospitals in the three register areas. It is difficult to examine this possibility because age of onset, number of episodes past the first, and calendar time are highly correlated. If all three variables are entered together as predictors, the models become ill-conditioned and nonsensical results are produced. In both Victoria and Denmark the number of psychiatric hospital beds was declining during the period of time under study in these cohorts. How-

ever, we feel this reduction was achieved by shortening the length of stay in the hospital, not by raising the threshold of severity required for admission. In these cohorts, median length of stay in the first versus the last of the 2-year followup periods was 56 versus 22 for Victoria, 37 versus 20 for Denmark, and 22 versus 17 for Salford. These changes are enough to account for the lowered number of beds in psychiatric hospitals.

There are some data relevant to the issue of historical trends in thresholds for hospitalization in the three register areas. A prior analysis of rehospitalization following only the first discharge was able to include calendar time as a covariate because the years of admission in that analysis had a greater range and there was no need to adjust for the number of the hospitalizations after the first (Eaton et al. 1992, Part I of this article). In that analysis the risk for rehospitalization following the first did not decline over the relevant time periods. Instead, the relative risks for rehospitalization following the first tended to rise over the period studied here in all three register areas. The rise in risk for rehospitalization is consistent with the development of the so-called "revolving-door" syndrome. Therefore, it seems unlikely that historical trends explain the temporal decline in rate of rehospitalization observed in tables 3 and 4 and in figures 4, 5, and 6.

What are the clinical implications of the results? In any given clinical situation, we cannot tell the individual diagnosed as having schizophrenia how many hospitalizations he or she will have to suffer through in the future. Nor can we say how long any given hospital episode will last. Nor can we say, for those who are discharged, how long they must wait before it is certain they will remain outside the hospital indefinitely. But we can say, based on these analyses, that schizophrenic patients will be less likely to be rehospitalized as time passes. The concept of progressive deterioration does not describe the process as accurately as progressive amelioration.

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